

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method of detecting ~~early stages of~~ Alzheimer's pathogenesis in vitro or in a transgenic model, comprising the steps of:

~~detecting a disruption in normal cellular distribution of a G-protein receptor kinase 5 (GRK5).~~

- a) estimating normal distribution of GRK5 in a cell;
- b) causing disruption in normal GRK5 distribution in the cell;
- c) estimating GRK5 distribution in the cell after step b);
- d) comparing the data of steps a) and c) to detect disruption in normal GRK5 distribution; and
- e) wherein a lower than normal content for membrane GRK5 indicates Alzheimer's pathogenesis.

Claim 2 (original): The method of Claim 1, wherein:

the disruption occurs in a prodromal stage of Alzheimer's disease.

Claim 3 (withdrawn): The method of Claim 1, wherein:

the disruption occurs in sub-cellular distribution of a GRK.

Claim 4 (canceled).

Claim 5 (withdrawn): The method of Claim 3, wherein:

the disruption comprises reduction in membrane-associated GRK.

Claim 6 (withdrawn): The method of Claim 1, wherein:

the disruption comprises increase in cytosolic GRK.

Claim 7 (original): The method of Claim 1, wherein:

the disruption is caused by a peptide.

Claim 8 (withdrawn): The method of Claim 7, wherein:

the peptide comprises β -amyloid.

Claim 9 (currently amended): The method of Claim 34, wherein:

the peptide comprises soluble β -amyloid 1-42 or 1-40.

Claim 10 (original): The method of Claim 9, wherein:

the concentration of soluble β -amyloid is in a nM range.

Claim 11 (original): The method of Claim 9, wherein:

the concentration of soluble β -amyloid is in a range of about 50 nM
- 500 nM.

Claim 12 (original): The method of Claim 1, wherein:

the detection step is carried out in brain cells.

Claim 13 (original): The method of Claim 12, wherein:

the brain cells comprise microglial cells.

Claim 14 (withdrawn): A method of detecting Alzheimer's pathogenesis, comprising:

detecting abnormal cellular accumulation of β -amyloid in a subject
suspect of having Alzheimer's disease.

Claim 15 (withdrawn): The method of Claim 14, wherein:

the abnormal accumulation is in a range of about 50 nM - 500 nM.

Claim 16 (withdrawn): The method of Claim 15, wherein:

the β -amyloid comprises soluble β -amyloid.

Claim 17 (withdrawn): The method of Claim 14, wherein:
the detection step is carried out in brain cells.

Claim 18 (withdrawn): The method of Claim 17, wherein:
the brain cells comprise microglial cells.

Claim 19 (withdrawn): A method of inhibiting GRK-GPCR interaction in a cell,
comprising:
pretreating a cell with a peptide.

Claim 20 (withdrawn): The method of Claim 19, wherein:
the peptide comprises β -amyloid.

Claim 21 (withdrawn): The method of Claim 19, wherein:
the peptide comprises soluble β -amyloid.

Claim 22 (withdrawn): The method of Claim 21, wherein:
the cell comprises a brain cell.

Claim 23 (withdrawn): The method of Claim 22, wherein:
the brain cell comprises a microglial cell.

Claim 24 (withdrawn): A method of inhibiting desensitization of GPCR in a cell, comprising:

pretreating a cell with a peptide.

Claim 25 (withdrawn): The method of Claim 23, wherein:

the peptide comprises β -amyloid.

Claim 26 (withdrawn): The method of Claim 23, wherein:

the peptide comprises soluble β -amyloid.

Claim 27 (withdrawn): The method of Claim 26, wherein:

the cell comprises a brain cell.

Claim 28 (withdrawn): The method of Claim 27, wherein:

the brain cell comprises a microglial cell.

Claim 29 (withdrawn): A method of preventing or suppressing Alzheimer's disease progression at prodromal or early stages, comprising:

correcting GRK dysfunction in cells.

Claim 30 (withdrawn): The method of Claim 29, wherein:

the GRK dysfunction is induced by β -amyloid.

Claim 31 (withdrawn): The method of Claim 30, wherein:

the β -amyloid comprises soluble β -amyloid.

Claim 32 (withdrawn): A method of correcting soluble β -amyloid induced GRK dysfunction in cells, comprising:

administering to a subject in need thereof a suitable amount of soluble β -amyloid antagonist.

Claim 33 (withdrawn): A vaccine comprising a β -amyloid analog for use as prophylaxis against β -amyloid induced reactions in a subject.

Claim 34 (currently amended): A method of detecting a disruption in normal cellular distribution of a G-protein receptor kinase 5 (GRK5) ~~by using a peptide~~, comprising the steps of:

- a) estimating normal distribution of GRK5 in a cell;
- b) treating the cell with soluble beta-amyloid peptide to disrupt normal GRK5 distribution;
- c) estimating GRK5 distribution in the cell after step b);

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d) comparing the data of steps a) and c) to detect disruption in
normal GRK5 distribution.